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EXAMINER	
LUCAS, ZACHARIAH	
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1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/507,232	GREEN ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-16, 24, 26-39* is/are pending in the application.

4a) Of the above claim(s) *24 and 26-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-16 and 35-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 September 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/8/04, 9/24/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 7-16, 24, and 26-39 are pending in the application.

Election/Restrictions

2. Applicant's election with traverse of Group II in the reply filed on September 24, 2007 is acknowledged. The traversal is on the ground(s) that the amended claims each relate to products and methods of using certain mutated retroviral nucleic acids. It is also noted that the claims have been amended to avoid the prior art cited in the Requirement for Restriction to break unity. Applicant asserted that each of the inventions pending in the application share the feature of the indicated nucleic acids, and should therefore be examined together. This is not found persuasive because, while the claims have been amended to avoid the prior art previously cited, the claims are still not considered to share Unity of Invention. In particular, the teachings of Wu et al., Virology 269:7-17 teach an ecotropic MLV envelope protein into which has been inserted a peptide ligand which is flanked by either side by at least one cysteine. See e.g., page 9, first full paragraph. Thus, examination in the present application is limited to the product of Group II, and a first method of using, which covers claims 7-16, and 35-39.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 24 and 26-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 24, 2007.

Information Disclosure Statement

4. The information disclosure statements (IDS) submitted on September 8, 2004, and September 24, 2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements have been considered by the examiner.

However, it is noted that no copies of non-patent literature cited in the September 2004 IDS have been provided to the Office as required by 37 CFR 1.98. It is noted that, MPEP 609(a)II indicates that the exception from the requirement to provide such copies applies to references cited in an earlier application filed under 35 U.S.C. § 120, but "does not apply to information which was cited in an international application under the Patent Cooperation Treaty." These references have therefore not been considered with the exception of the Kasahara reference cited in the restriction requirement.

Drawings

5. The drawings are objected to because portions of Figure 8 are illegible. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be

labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 13-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims read on a method for the alteration of retroviral tropism comprising the introduction into a retroviral genome the nucleic acid of claim 7, and thereby producing a pseudovirus having altered tropism. It is not clear what is being claimed. The teachings of the art indicate that a pseudovirus is a virus incorporating the envelope protein of a different virus. See e.g., Burns et al., PNAS 90:8033-37, at 8033 left column. Further, the specification (page 9) teaches that the pseudovirus is produced through the expression of the chimeric envelope protein of the invention in a cell also expressing the packing construct LGRNL, which encodes a VSV G protein. Burns, supra., page 8034. From the teachings of the claims and the application, it is not clear what is meant in the claims by reference to the pseudovirus. It is not clear if the resulting viral particles require the presence of a different viral envelope protein in the place of, or in combination with, the chimeric envelope protein, or if the chimeric envelope protein is considered by the Applicant to serve as a foreign envelope protein.

Further the claims are also ejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In particular, the teachings of the application, and the understanding of what comprises a pseudotype virus in the art, indicates that such a virus is not made merely through the introduction of a mutation into a viral envelope protein in a viral genome. Additional steps are required to produce the referenced pseudoviral particles.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This is a New Matter rejection. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 13 is treated as representative. This claim has been amended to read on a method for altering viral tropism comprising introducing into the genome of a retrovirus a nucleic acid encoding a retroviral ecotropic envelope protein modified to include a peptide ligand as described in claim 7, and thereby producing a pseudovirus. There is no descriptive support for such a method in the application. The application discloses only the production of a pseudovirus comprising the introduction into a cell of a nucleic acid encoding the chimeric envelope protein and a packaging construct such as is disclosed on page 9 of the application. The indicated claims are therefore rejected for lacking descriptive support.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

11. Claims 7, 8, 10, 11, 35-37, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Wu et al. (Virology, 269:7-17). Claims 7 and 32-37 read on a nucleic acid encoding a chimeric retrovirus envelope protein comprising an ecotropic envelope protein and a heterologous short peptide ligand inserted within the protein coding sequence, wherein the peptide ligand is flanked by at least one cysteine on each side (optionally with additional amino acids between the ligand and the cysteines). Claim 35 requires that the ecotropic envelope protein is an MLV envelope protein. Claim 37 requires that the peptide ligand is an RGD ligand. Claims 8 and 39 read on vectors (esp. a retroviral vector) comprising the nucleic acid, and claims 10 and 11 read on a recombinant retroviral particle comprising the nucleic acid, with claim 11 requiring that the retroviral particle be capable of infecting a mouse cell.

Such nucleic acids, vectors, and retroviral particles are disclosed by Wu. On page 9 of the reference, Wu discloses that an RGD peptide ligand was inserted into a site in an ecotropic MLV

envelope protein where the peptide was flanked on either side by at least one cysteine residue. The reference teaches, on page 14 (section entitled "Envelope protein expression plasmids"), that the peptide ligand coding sequence was inserted into a nucleic acid encoding the ecotropic MLV envelope protein. Page 15 of the reference teaches the production of retroviral vectors comprising the nucleic acids encoding the mutant envelope proteins. Further, on pages 10-11, the reference teaches that the viral particles comprising one of the mutants meeting the limitations of the present claims (wherein the peptide ligand was inserted between residues 78 and 79 of the wild-type envelope protein) was capable of infecting murine cells. The reference therefore anticipates the indicated claims.

12. Claims 7, 8, 35-37, and 39 are rejected under 35 U.S.C. 102(b) as being anticipated by Kingsman (U.S. 6,132,731). The claims have been described above.

Kingsman teaches a nucleic acid encoding a chimeric ecotropic MLV envelope protein into which a RGD peptide ligand flanked by cysteines has been inserted. Columns 7-8. The reference therefore anticipates the indicated claims.

13. Claims 7, 8, 35, 37, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Albritton et al. (U.S. 6,448,390). Claims 7, 8, 35, and 37 have been described above. Claim 38 is directed to the nucleic acid sequence of claim 7 wherein the peptide ligand is into a conserved domain in the envelope protein.

Albritton teaches nucleic acids (and vectors comprising such) encoding mutated envelope proteins of an ecotropic MLV comprising an insertion between amino acid residues 6 (serine)

and 7 (proline) the cyclic nonapeptide CDCRGDCFC as a peptide ligand. Columns 41-42. With respect to claim 38, it is noted that Albritton does not specifically indicate that the ligand was inserted into a conserved region. However, the teachings in the art indicate that the position into which the ligand was inserted is conserved in the murine leukemia viruses. See e.g. Battini et al., J Virol 66:1468-75 (at page 1472, Figure 2- identifying the Ser6 and Pro7 residues as conserved amino acids). The reference therefore anticipates the indicated claims.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 9, 10, 11, and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Albritton as applied to claims 7, 8, 35, 37, and 38 above. Claims 10 and 11 have been described above. Claim 9 reads on a vector comprising the nucleic acid described above and, in addition, also encodes a therapeutically useful polypeptide. For the purposes of this rejection, claims 13-15 will be read as the production of a retroviral vector wherein the viral envelope protein has been modified as described in the claim. Reference to the pseudovirus in the claim is interpreted as including any virus particle comprising a non-native viral envelope protein, such as a modified version of the virus' own envelope protein. Claim 16 reads on the method of claim 13, wherein the peptide ligand is inserted into a conserved region of the viral envelope protein.

The teachings of Albritton have been described above. The reference teaches a nucleic acid encoding a chimeric ecotropic MLV envelope protein as described by the present claims, and indicates that retroviral particles expressing the chimeric protein are capable of infecting and thereby delivering genes to targeted human cells. Columns 41-42. Further, the reference also indicates that alternatives to the pseudoviral particles used in the examples are retroviral particles in which encode the modified envelope proteins. Columns 3-4 and 20-21. Further, the reference also teaches that these vectors are useful for the delivery of genes encoding therapeutically useful polypeptides. Column 21-22. Thus, the claimed vectors and methods would have been obvious to those of ordinary skill in the art based on the teachings of the reference.

16. Claim 38 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wu et al. (supra), in view of the teachings of Yamada et al. (Biochemistry 33:11678-83), and Curiel et al., (U.S. 2002/0081280). This claim is directed to the nucleic acid sequence of claim 7 wherein the peptide ligand flanked by at least one cysteine on either side is inserted into a conserved domain in the envelope protein.

The teachings of Wu have been described in part above. It is noted that this reference teaches insertions of a peptide ligand into conserved regions of the viral envelope protein. See e.g., page 9, Table 1. However, the reference indicates that the viruses having such insertions were not capable of infecting human cells expressing the target receptor. Page 12. However, the reference suggests that the problem may be overcome through the use of flanking cysteine residues. Page 14. Moreover, other teachings in the art indicate both that the use of such flanking cysteines improves the operation of the inserted RGD peptide ligands (Yamada, pages 11681-

82), and that other viral envelope proteins expressing such peptides were capable of infecting cells with the target receptor (Curiel, page 18, Example 26). Based on the suggestion by Wu, and the teachings of the other references, it would have been obvious to those of ordinary skill in the art to have modified the conservative insertions of Wu through the inclusion of flanking cysteines so as to improve the performance of the chimeric envelope proteins described by Wu. The additional teachings in the art would have provided those of ordinary skill in the art with a reasonable expectation of success in the making of the nucleic acids suggested by Wu. The combined teachings of these references therefore render the claimed invention obvious.

17. Claims 9-11, 13-15, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kingsman as applied against claims 7, 8, 35-37, and 39 above, and further in view of Anderson et al. (U.S. 5,985,655). Claims 9-11 and 13-15 have been described above. Claim 39 reads on a vector comprising the nucleic acid of claim 7, wherein the vector is a retroviral vector.

The teachings of Kingsman have been described in part above. The reference also teaches that pseudoviral particles expressing the chimeric envelope proteins were capable of binding to and transducing human cells expressing the receptor for the inserted peptide ligand. Columns 9-10. The reference also suggests the inclusion of therapeutic genes in the resulting viral vectors. Column 4, lines 36-50). However, while the reference teaches the retroviral vectors, it does not teach that the vectors encode the chimeric envelope protein.

Anderson also teaches retroviral viral particles comprising chimeric envelope proteins changing the viral tropism. Columns 1-2. The reference teaches that useful retroviral particles may encode the chimeric envelope protein (col. 1, lines 58-63, and col. 6, lines 27-30) as well as

including desirable heterologous genes (i.e. therapeutic genes- column 6, lines 46-65). From the teachings of this reference, it would have been obvious to those of ordinary skill in the art that the retroviral vectors of this reference and pseudoviral particles of Kingsman are functional equivalents for the delivery of genes to cells targeted by the ligands incorporated into the chimeric envelope proteins. It would therefore have been obvious that the retroviral vectors of Kingsman may be made to include the gene that encodes the chimeric envelope protein. Moreover, because the Kingsman reference indicates that MLV viral particles including the chimeric envelope proteins disclosed therein were effective for targeting human cells, those of ordinary skill in the art would have had a reasonable expectation of success in the making of retroviral particles encoding the chimeric protein as a delivery vector. The combined teachings of these references therefore render the claimed invention obvious.

18. Claims 9-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kingsman as applied against claims 7, 8, 35-37, and 39 above, and further in view of Paul et al. (U.S. 5,736,387) and Panda et al. (Virology 273:90-100). Claims 9-11, and 13-15 have been described above. Claim 12 reads on the vector of claim 10, wherein the vector cannot infect a mouse cell.

The teachings of Kingsman have been described above.

Paul, like the Anderson reference above, also teaches retroviral vectors with chimeric (albeit, with different types of mutations from those of Kingsman and Anderson) envelope proteins, and indicates that the vectors may include the genes encoding such proteins. Abstract, column 6 lines 45-53. Moreover, the reference teaches that the resulting vectors are useful for the same purpose as the vectors of Kingsman (i.e. for the delivery of therapeutically useful genes).

See e.g., columns 26-27. In addition, the reference also indicates that it may be useful to modify the retroviral vectors such that they are no longer capable of infecting the cells expressing the wild-type viral envelope protein receptor. Column 18. The reference teaches that one means for accomplishing this is to inert a mutation disrupting the ability of the protein to bind that native envelope protein receptor. Id., lines 44-50. Such mutations for the MuLV envelope protein are disclosed in the art. See e.g., Panda, pages 90 and 95. In view of these teachings, it would have been obvious to further modify the vectors and nucleic acids of Kingsman as suggested by the teachings of Paul and Panda. The combined teachings of these references therefore render the claimed invention obvious.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Z. Lucas/
Patent Examiner, AU 1648